Docket No.: 68115(46590)
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Shigeo Yanai et al.

Application No.: 10/549,893 Confirmation No.: 7166

Filed: September 16, 2005 Art Unit: 1615

For: RELEASE CONTROL COMPOSITIONS Examiner: A. Sasan

AMENDMENT AFTER FINAL ACTION UNDER 37 C.F.R. 1.116

MS RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir/Madam:

INTRODUCTORY COMMENTS

In response to the Office Action dated November 24, 2009, finally rejecting claims 23 and 27, please amend the above-identified U.S. patent application as follows:

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 3 of this paper.

An Extension of Two (2) months of time for reply is respectfully requested.

AMENDMENTS TO THE CLAIMS

Applicants respectfully request that the application be amended without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows.

1 - 22. (canceled)

23. (Currently amended) A controlled release composition for oral administration, wherein

(A) a core containing (1) (+)-6-(7-hydroxy-6,7-dihydro-5Hpyrrolo[1,2-c]imidazol-7-y1)-N-methy1-2-n- aphthamide or a salt thereof, and (2) ~~a hydrophilic polymer selected from~~ hydroxypropylcellulose, and low-substituted hydroxypropylcellulose as a hydrophilic polymer, wherein an inert carrier particle is coated with a coating layer comprising (1) (+)-6-(7-hydroxy-6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-7-yl)-N-methyl-2-naphthamide or a salt thereof, and (2) ~~a hydrophilic polymer selected from~~ hydroxypropylcellulose, and low-substituted hydroxypropylcellulose as a hydrophilic polymer, which is coated with

(B) a coating layer containing (1) methacrylic acid copolymers as an enteric coating agent, (2) talc as a lubricant, and (3) a plasticizer selected from polyethylene glycol and triethyl citrate, wherein the core is in a granule form having the average particle diameter of from about 50 to about 2000 μm.

24 - 26. (canceled)

27. (Previously amended) The controlled release composition according to claim 23, which is used for prevention or treatment of prostate cancer or breast cancer.

28 - 35. (canceled)

36. (New) A capsule preparation comprising the controlled release composition according to claim 23.

REMARKS

Claims 23 and 27 are pending in the instant application. Claim 23 is amended. The amendment is supported throughout the specification, for example on page 57, lines 20-22, in reference examples 1 and 2, and in examples 5-8, 12, and 13. Claim 36 has been added. The claim is supported, for example, on page 65, lines 10-14 of the specification, and in examples 7, 8, and 13. No new matter is added by the amendments.

Withdrawal of Rejections

Applicant thanks the Examiner for withdrawal of the prior rejection of the claims for allegedly being unpatentable over Tasaka et al. (WO 02/40484) in view of Mazer et al. (US 5,160,742).

Rejection of claims under 35 U.S.C. §103

The Office Action has rejected claims 23 and 27, all of the claims that were pending in the application, for under 35 U.S.C. 103(a) for allegedly being unpatentable over Tasaka et al. (WO 02/40484) in view of Mazer et al. (US 5,160,742) and further in view of Samejima et al. (US 5,068,112).

Applicant respectfully disagrees. The references, even in combination, fail to make obvious the instantly claimed invention.

Applicant points to the figures of the instant application showing the substantial change in plasma concentration over time of the active ingredient depending on the formulation of the active ingredient. As shown in Figure 1, administration of homogeneous formulations results in an abrupt peak plasma concentration with a rapid decrease in plasma concentration. This is distinct from the slow release formulations shown in Figures 2-6. However, it is noted that the plasma concentration over time varies substantially depending on the specific composition used, even within the context of the claimed invention, e.g., compare preparations 6, 10, and 14 all administered to dogs. The specific release profiles could not be predicted by the combination of the

teachings of the cited art. The controlled release composition containing such a core of the active ingredient can improve blood concentration of the active ingredient and sustainability thereof as shown in Figs. 4 and 6 (Preparation 11 and 16) in the present specification.

The Court has addressed the issue of obviousness in chemical cases since the decision of KSR. Specifically the Court stated:

> While the KSR Court rejected a rigid application of the… TSM test in an obviousness inquiry, the Court acknowledged **the importance of identifying 'a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination**.
>
> When there is a design need or market pressure to solve a problem and there is **a finite number of identified, predictable solutions**, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp." *KSR*, 127 S. Ct. at 1732. * * * That is not the case here. Rather than identify predictable solutions for antidiabetic treatment, the prior art disclosed a broad selection of compounds any one of which could have been selected as a lead compound for further investigation. Significantly, the closest prior art compound (compound b, the 6-methyl) exhibited negative properties that would have directed one of ordinary skill in the art away from that compound. *Takeda Chemical Industries Ltd. v. Alphapharm Pty.* 492 F.3d 1350 (Fed. Cir. 2007) [emphasis added]

The Office Action provides no reason that would have prompted one of ordinary skill to combine the elements in the way that the claimed new invention does. Release of the active agent into the blood depends not only on the components of the composition, but also the way in which the components are combined. Again, compare the results shown in Figure 1 with the results in the remaining figures. Although the components are similar, the way that the components are combined is equally important in determining release properties. The various methods to prepare formulations for oral administration provides further complexity to the number of “solutions” to any “problem” in the prior art.

Each of the references provides a broad list of possible components for formulation of the active agents and multiple methods for preparation of dosage formulations. Even if the references were to disclose each of the components of the instantly claimed compositions, which they do not, there can be no motivation to combine them as instantly claimed.

Mazer requires the use of two coating layers, the first layer including a prolamine. No prolamine layer is required in the instantly claimed compositions. Modification of Mazer to not include a prolamine coating would be contrary to the teachings of Mazer; therefore, the modification cannot be obvious. Moreover, the coating of Mazer is optimized for use with beta-lactam antibiotics. Therefore, it would not be obvious to modify a reference for the delivery of an antibiotic to provide for the delivery of a chemotherapeutic agent.

Similarly, Samejima requires the use of ethyl cellulose in the composition. No ethyl cellulose is required in the instantly claimed compositions. Modification of Samejima to not include a ethyl cellulose would be contrary to the teachings of Samejima; therefore, the modification cannot be obvious.

In view of the above reasons, the rejections should be withdrawn.

Further, the claims have been amended to recite that the composition includes both hydroxypropylcellulose and low-substituted hydroxypropylcellulose. Low-substituted hydroxypropylcellulose is not taught by any of the references. Moreover, there can be no motivation based on the teachings of the cited references to further include a low-substituted hydroxypropylcellulose in a composition containing hydroxypropylcellulose. particularly inclusion of the hydroxypropylcellulose and the low-substituted hydroxypropylcellulose in the core of a drug formulation.

Withdrawal of the rejections is respectfully requested.

FEE AUTHORIZATION

The Commissioner is hereby authorized to charge Deposit Account No. 04-1105, Docket No. 68115(46590) the fee for a two month extension of time for reply, large entity. It is believed that there is no further fee due with this response. However, if a further fee is due with this response, or any other fee filed by this firm in relation to this application, the Commissioner is hereby authorized to charge the above named Deposit Account. Refund of any overpayment is respectfully requested.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: April 22, 2010

Respectfully submitted,
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